

## WHAT IS CLAIMED IS:

1. A method of enhancing active agent localization at a target site in a mammalian recipient, which method comprises:

administering to the recipient a first conjugate comprising a targeting moiety and a biotin, whereupon the first conjugate localizes to the target site;

administering to the recipient avidin or streptavidin; and

thereafter administering to the recipient a second conjugate comprising biotin, a linker resistant to biotinidase cleavage and an active agent, wherein second conjugate localization at the target site is enhanced as a result of prior localization of the first conjugate.

2. A method of claim 1 wherein the targeting moiety is proteinaceous.

3. A method of claim 1 wherein the targeting moiety is an oligonucleotide, a peptide, a polypeptide, a cytokine, a monoclonal antibody, a monovalent fragment thereof.

4. A method of claim 3 wherein the monoclonal antibody is a human, a humanized or a chimeric monoclonal antibody.

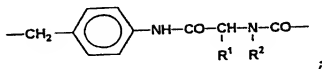
5. A method of claim 3 wherein the monoclonal antibody or fragment thereof is reactive with an antigen recognized by the antibody NR-LU-10.

6. A method of claim 1 wherein the active agent is selected from the group consisting of

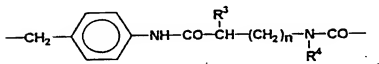


wherein a linker L is selected from the group comprising:

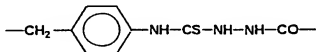
1) a D-amino acid-containing linker of the formula



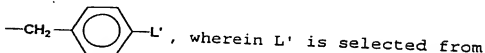
2) a linker of the formula



3) a linker of the formula



4) a linker of the formula



the group comprising:

a)  $\text{—NH—CO—(CH}_2\text{)}_n\text{—O—}$  ;

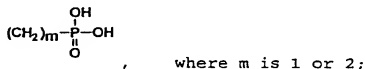
b)  $\text{—NH—}$  ;

c)  $\text{—NH—CO—CH}_2\text{—N—R}^{1'}$  ;

d)  $\text{—NH—CS—NH—}$  ; and

e)  $\text{—NH—CO—(CH}_2\text{)}_n\text{—NH—}$ ,

wherein R<sup>1</sup> is hydrogen, lower alkyl; lower alkyl substituted with one or more hydrophilic groups including  $(\text{CH}_2)_m\text{—OH}$ ,  $(\text{CH}_2)_m\text{—OSO}_3$ ,  $(\text{CH}_2)_m\text{—SO}_3$ , and

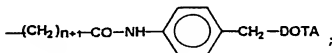


glucuronide-substituted amino acids; or other glucuronide derivatives;

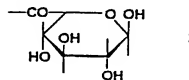
$R^2$  is hydrogen; lower alkyl; substituted lower alkyl having one or more substituents selected from the group comprising hydroxy, sulfate, and phosphonate; or a hydrophilic moiety;

$R^3$  is hydrogen; an amine; a lower alkyl; a hydroxy-, sulfate- or phosphonate-substituted lower alkyl; a glucuronide; or a glucuronide-derivatized amino acid;

$R^4$  is hydrogen, lower alkyl or

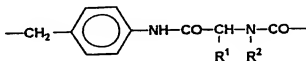


$R'$  is hydrogen;  $-(CH_2)_2-\text{OH}$  or a sulfate or phosphonate derivative thereof; or



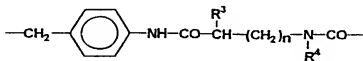
$R''$  is a bond or  $-(CH_2)_n-\text{CO}-\text{NH}-$ ; and  $n$  ranges from 0-5.

14. A method of claim 13 wherein L is a D-amino acid-incorporating linker of the formula



15. A method of claim 14 wherein  $R^1$  is  $\text{CH}_3$  and  $R^2$  is H.

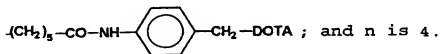
16. A method of claim 13 wherein L is a linker of the formula



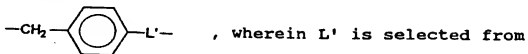
17. A method of claim 16 wherein  $R^3$  is hydrogen;  $R^4$  is  $CH_3$ ; and  $n$  is 4.

18. A method of claim 16 wherein  $R^3$  is hydrogen;  $R^4$  is  $CH_3$ ; and  $n$  is 0.

19. A method of claim 16 wherein  $R^3$  is hydrogen;  $R^4$  is

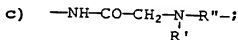


20. A method of claim 13 wherein  $L$  is a linker of the formula



the group comprising:

- a)  $-NH-CO-(CH_2)_n-O-$  ;
- b)  $-NH-$  ;



- d)  $-NH-CS-NH-$  ; and

e)  $-NH-CO-(CH_2)_n-NH-$  or a bis-DOTA derivative thereof.